510(k) SUMMARY

APR 0 4 2014

General Information

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Device Name: *artus*® C. difficile QS-RGQ MDx Kit

Trade Name: *artus*® C. difficile QS-RGQ MDx Kit
Common Name: C. difficile nucleic acid amplification test assay
Classification: Class II

Predicate Device

Manufacturer	Product Name	510(k) No.
Quidel	Quidel Molecular Direct C. difficile Assay	K123998

Device Description

The *artus* C. difficile QS-RGQ MDx Kit assay uses PCR to generate an amplified product from the *tcdA* and *tcdB/tcdBv* genes of toxigenic *C. difficile* DNA in clinical specimens. Samples are extracted and prepared using the QIAsymphony SP instrument with the QIAsymphony DSP Virus/Pathogen Mini Kit, followed by assay setup on the QIAsymphony AS. Amplification and detection are carried out using the *artus* C. difficile QS-RGQ MDx Kit with the Rotor-Gene Q MDx (RGQ MDx) and Rotor-Gene AssayManager software. The presence of a toxigenic *C. difficile* target sequence is indicated by the fluorescent signal generated through the use of fluorescently labeled oligonucleotide probes. The probes do not generate a signal unless they are specifically bound to the amplified product. The amplification cycle at which fluorescent signal is

detected by the RGQ MDx is inversely proportional to the toxigenic *C. difficile* DNA target concentration present in the original specimen. A bacterial species unrelated to toxigenic *C. difficile* is introduced into each specimen during sample preparation to serve as an internal control. The internal control bacteria are lysed simultaneously with toxigenic *C. difficile* in the specimen, and amplified in the same reaction as the *C. difficile* targets using PCR, and serve to demonstrate that the entire assay process has proceeded correctly for each specimen.

Intended Use

The *artus* C. difficile QS-RGQ MDx Kit is an *in vitro* polymerase chain reaction (PCR) assay for use on the QIAsymphony RGQ MDx system for the qualitative detection of toxigenic *Clostridium difficile* toxin A and toxin B genes in human liquid or soft stool specimens from patients suspected of having *Clostridium difficile* associated disease. The test is intended to be used directly on patient samples.

The *artus* C. difficile QS-RGQ MDx Kit is intended to be used to aid in diagnosis of *Clostridium difficile* infection.

Comparison of the *artus*® C. difficile QS-RGQ MDx Kit and the Predicate Device

The *artus*® C. difficile QS-RGQ MDx Kit is substantially equivalent to the predicate device:

- K123998: Quidel Molecular Direct C. difficile Assay

Similarities and differences between the *artus*® C. difficile QS-RGQ MDx Kit (72) and the predicate device are shown in Table 1.

Table 1: Comparison of the *artus*® C. difficile QS-RGQ MDx Kit with the predicate device.

Characteristic	Device	Predicate
Name	*artus* C. difficile QS-RGQ MDx Kit	Quidel Molecular Direct C. difficile Assay
510(k) No.	TBD	K123998
Regulation	866.3130	866.3130
Product Code	OZN	OZN
Device Class	Class II	Class II
Similarities		
Intended Use	The *artus* C. difficile QS-RGQ MDx Kit is an *in vitro* polymerase chain reaction (PCR) assay for use on the QIAsymphony RGQ MDx system for the qualitative detection of toxigenic *Clostridium difficile* toxin A and toxin B genes in human liquid or soft stool specimens from patients suspected of having *Clostridium difficile* associated disease. The test is intended to be used directly on patient samples. The *artus* C. difficile QS-RGQ MDx Kit is intended to be used to aid in diagnosis of *Clostridium difficile* infection.	The Quidel Molecular Direct C. difficile Assay is a qualitative, multiplexed *in vitro* diagnostic test for the direct detection of toxin A gene (*tcdA*) or toxin B gene (*tcdB*) sequences of toxigenic strains of *Clostridium difficile* from unformed (liquid or soft) stool specimens collected from patients suspected of having *Clostridium difficile*-Associated Disease (CDAD). The Quidel Molecular Direct C. difficile Assay is a real-time PCR test and utilizes proprietary sample preparation with fluorescently labeled primers and probes. The assay can be performed using either the Life Technologies QuantStudio® Dx; the Applied Biosystems 7500 Fast Dx, or the Cepheid SmartCycler II, to detect the toxin gene sequences associated with toxin-producing *C. difficile* strains. The assay is intended to be performed directly on CDAD-suspected stool specimens, and is indicated for use as an aid in the diagnosis of CDAD.
Specimen Type	Liquid or soft stool	Unformed (liquid or soft) stool

Characteristic	Device	Predicate
Assay Targets	Toxin A gene (*tcdA*) Toxin B gene (*tcdB* and *tcdBv*)	Toxin A gene (*tcdA*) Toxin B gene (*tcdB*)
Amplification and Detection Technology	Real-time PCR DNA amplification	Real-time PCR DNA amplification
Differences		
Assay Controls	Positive Control, Negative Control and Internal Control included in the kit.	Process Control included in the kit. Positive and Negative Controls not included in kit; separate control kit available for sale.
Nucleic Acid Extraction and Assay Setup	Assay uses the QIAsymphony SP/AS for automated sample preparation and assay setup.	Assay uses proprietary sample preparation buffer and manual assay setup.
Amplification and Detection Instrument System	Assay uses the Rotor-Gene Q MDx.	Assay can be performed using either the: • Life Technologies QuantStudio Dx • Applied Biosystems 7500 Fast Dx • Cepheid SmartCycler II

The differences between the *artus* C. difficile QS-RGQ MDx Kit and Quidel Molecular Direct C. difficile assays are primarily centered around the control strategy and instrumentation. These differences do not affect substantial equivalency of the *artus* C. difficile QS-RGQ MDx Kit and the Quidel Molecular Direct C. difficile Assay. Both assays detect toxigenic *C. difficile*, and the assays have comparable intended uses. The differences noted above do not change the intended use and do not raise questions of safety and effectiveness.

Performance Characteristics - Non-Clinical Studies

Analytical Sensitivity (Limit of detection)

The limit of detection (LoD) was assessed for the *artus* C. difficile QS-RGQ MDx Kit using 3 toxigenic *Clostridium difficile* strains: NAP-1/BI/027 strain, toxinotype III A+B+ (ATCC® BAA-1870); 1470 strain, toxinotype VIII A-B+ (ATCC 43598); and VPI 10463 strain, toxinotype 0 A+B+ (ATCC 43255). The LoD is defined as the toxigenic *C. difficile* bacterial titer (CFU/mL) detected with a probability of 95% or greater and was determined by probit analysis. The results, representative of the analytical sensitivity of the artus C. difficile QS-RGQ MDx Kit, are summarized in Table 2.

Table 2: Limit of Detection

Strain	LoD (95%CI)
C. difficile NAP1 ATCC BAA-1870, strain:4118	7.9 CFU/mL (6.1-15.0)
C. difficile 1470 ATCC 43598, strain:1470	11.2 CFU/mL (8.7-16.8)
C. difficile 10463 ATCC 43255, strain:10463	2.8 CFU/mL (2.1-4.2)

Analytical Reactivity

The analytical reactivity of the *artus* C. difficile QS-RGQ MDx Kit was assessed to determine whether the kit could detect a broad range of toxigenic *C. difficile* strains representing temporal and geographical diversity. A total of 27 strains and characterized clinical isolates were diluted in TE buffer to 2–3x LOD of the reference strain and tested with the *artus* C. difficile QS-RGQ MDx Kit. *C. difficile* target was detected in all strains tested Table 3.

Table 3: Strains Tested in Analytical Reactivity

Name	Strain	Toxinotype	Origin
ATCC 17857	870	O	unknown
ATCC 17858	1253	N/A	unknown
ATCC 43594	W1194	N/A	Human feces; Belgium
ATCC 43596	545	N/A	Human feces; Belgium
ATCC 43599	2022	N/A	Human feces; Belgium
ATCC 43600	2149	N/A	Human feces; Belgium
ATCC 51695	BDMS 18AN	N/A	Becton Dickinson Microbiology Systems, Johns Hopkins Univ. Hosp. Lab
ATCC 700792	14797-2	N/A	Human feces; Michigan, USA
ATCC 9689	90556-M6S	O	unknown
ATCC BAA-1382	630	X	Switzerland
ATCC BAA-1805	N/A	III	unknown
ATCC BAA-1871	4111	O	Human; New Jersey, USA
ATCC BAA-1872	4206	O	Human; Maine, USA
ATCC BAA-1873	5283	O	Human; New York, USA
ATCC BAA-1874	4205	O	Human; Oregon, USA
ATCC BAA-1875	5325	V	Human; Georgia, USA
ATCC BAA-2155	LBM 0801058	N/A	Human; New Mexico, USA
ATCC BAA-2156	LBM 0801040	N/A	Human; Cambridge UK
CCUG 20309	8864	X	Birmingham, UK
Illinois VA Hospital isolate 278	N/A	II	Illinois, USA
Illinois VA Hospital isolate 464	N/A	IV	Illinois, USA
Illinois VA Hospital isolate	N/A	VIII	Illinois, USA

Name	Strain	Toxinotype	Origin
4092			
Illinois VA Hospital isolate 5572	N/A	VIII	Illinois, USA
Illinois VA Hospital isolate 3430	N/A	IX	Illinois, USA
Illinois VA Hospital isolate 1753	N/A	XII	Illinois, USA
Illinois VA Hospital isolate 5090	N/A	XXI	Illinois, USA
Illinois VA Hospital isolate 3130	N/A	XXII	Illinois, USA

Cross-Reactivity and Microbial Interference

A panel of microorganisms that may be present in patient specimens was tested to determine whether these microorganisms interfered with the detection of *tcdA* or *tcdB* targets or were cross-reactive with the *artus* C. difficile QS-RGQ MDx Kit. Organisms were tested at a target concentration of approximately 1 x 10^6 CFU/ml for bacteria and fungi or ≥1 x 10^5 units/ml for viruses separately in the presence of 2–3x LOD of each of three *C. difficile* strains: NAP-1/BI/027 strain, 1470 strain, and VPI 10463 strain. None of the potential interfering organisms cross-reacted or interfered with the detection of any of the 3 *C. difficile* strains by the *artus* C. difficile QS-RGQ MDx Kit (Table 4). Cross-reactivity for *Clostridium botulinum* was analyzed *in silico* and predicted no cross reactivity or microbial interference for the *artus* C. difficile QS-RGQ MDx Kit.

Table 4: Organisms Tested in Cross Reactivity and Microbial Interference

Organism Tested	Source ID
Abiotrophia defectiva	ATCC 49176
Acinetobacter baumannii	ATCC 19606
Aeromonas hydrophila	ATCC 7966
Alcaligenes faecalis subsp. *faecalis*	ATCC 15554
Bacillus cereus	ATCC 13472
Bacteroides fragilis	ZMC 0601533

Organism Tested	Source ID
Campylobacter coli	ATCC 43479
Campylobacter coli	ATCC 33559
Campylobacter jejuni subsp. *jejuni*	ATCC 33292
Candida albicans	ATCC 10231
Citrobacter freundii	ATCC 8090
Clostridium bifermentans	ATCC 638
Clostridium butyricum	ATCC 19398
Clostridium haemolyticum	ATCC 9650
Clostridium novyi	ATCC 19402
Clostridium orbiscindens	ATCC 49531
Clostridium perfringens	ATCC 13124
Clostridium scindens	ATCC 35704
Clostridium septicum	ATCC 12464
Clostridium sordellii	ATCC 9714
Clostridium difficile (non-toxigenic)	ATCC 43593
Clostridium difficile (non-toxigenic)	ATCC 43601
Clostridium sporogenes	ATCC 15579
Edwardsiella tarda	ATCC 15947
Enterobacter aerogenes	ATCC 13048
Enterobacter cloacae	ATCC 13047
Enterococcus faecalis (vanB)	ATCC 51299
Escherichia coli	ATCC 23511
Escherichia coli O157:H7	ATCC 700927
Helicobacter pylori DNA	ATCC 43504D-5
Klebsiella oxytoca	ATCC 33496
Lactobacillus acidophilus	ATCC 4356
Listeria monocytogenes	ZMC 0801534
Peptostreptococcus anaerobius	ATCC 27337
Plesiomonas shigelloides	ATCC 14029
Porphyromonas asaccharolytica	ATCC 25260
Prevotella melaninogenica	ATCC 25845
Proteus mirabilis	ATCC 25933
Providencia alcalifaciens	ATCC 9886
Pseudomonas aeruginosa	ATCC 35554
Salmonella choleraesuis (Typhimurium)	ATCC 14028
Salmonella enterica subsp. *arizonae*	ATCC 13314
Salmonella enterica subsp. *enterica*	ATCC 7001
Serratia liquefaciens	ATCC 27592
Serratia marcescens	ATCC 13880
Shigella boydii	ATCC 9207
Shigella dysenteriae	ATCC 11835

Organism Tested	Source ID
Shigella sonnei	ATCC 29930
Staphylococcus aureus	ATCC 43300
Staphylococcus epidermidis	ATCC 14990
Streptococcus agalactiae	ATCC 27541
Vibrio parahaemolyticus	ATCC 17802
Adenovirus	ZMC 0810110 CF
Rotavirus	ZMC 0810041 CF
Norovirus	ZMC 0810086 CF
Enterovirus	ZMC 0810047 CF
Echovirus	ZMC 0810023 CF
Coxsackie virus	ZMC 0810075 CF
Cytomegalovirus	ZMC 0810003 CF
Human Genomic DNA	Promega G3041

Precision

The precision of the *artus* C. difficile QS-RGQ Kit was assessed using a 7-member panel consisting of 2 *C. difficile* strains: NAP-1/BI/027 strain, toxinotype III A+B+ (ATCC BAA-1870) and 1470 strain, toxinotype VIII A-B+ (ATCC 43598). Panel members were initially diluted in TE buffer then tested in Buffer ATL containing negative stool matrix with a single strain present (NAP-1/BI/027 or 1470) at 3 concentrations; positive (approximately 2–3x LoD), low positive (1x LoD), and high negative (<1x LoD). A seventh panel member (negative) was prepared using TE buffer only and also tested in Buffer ATL containing negative stool matrix. The data obtained were used to determine the mean C_T, standard deviation (SD) and the coefficient of variation (%CV) for each target and the internal control.

For the within laboratory repeatability study, the seven-member panel was tested in replicates of three, once a day for a total of twelve days (for a total of 262 data points for the 12 runs). The testing was conducted by two operators using one instrument (QS/AS RGQ MDx) and one reagent kit lot (Table 5).

Table 5: Within Laboratory Repeatability Study Results

	Internal Control			*tcdA*			*tcdB*		
Panel Member	**MEAN**	**STDEV**	**%CV**	**MEAN**	**STDEV**	**%CV**	**MEAN**	**STDEV**	**%CV**
NAP1 Positive	29.78	0.49	1.64%	30.84	0.47	1.52%	33.58	0.64	1.91%
NAP1 Low Positive	30.07	0.55	1.82%	32.19	0.99	3.08%	34.92	0.68	1.94%
NAP1 High Negative	29.99	0.72	2.41%	34.21	0.91	2.66%	36.18	0.23	0.64%
1470 Positive	29.85	0.52	1.73%	30.95	0.55	1.78%	33.72	0.45	1.33%
1470 Low Positive	29.89	0.41	1.39%	32.14	0.65	2.03%	35.13	0.63	1.80%
1470 High Negative	29.92	0.53	1.76%	34.14	0.66	1.92%	36.39	0.03	0.07%
Negative	30.00	0.44	1.46%	N/A	N/A	N/A	N/A	N/A	N/A

To measure site-to-site reproducibility, the 7-member panel was run by 2 users at each of 3 sites (IMDx and 2 external sites). Each of the 2 users performed 5 runs on alternating testing days. Panel members were tested in replicates of 3 that were randomized and blinded to the user. A single QIAsymphony RGQ instrument system and one lot of the *artus* C. difficile QS-RGQ Kit were used at each site to conduct the study (Table 6).

Table 6: Site-to-Site Reproducibility Study Results

			Internal Control			*tcdA*			*tcdB*		
Strain	**Panel Member**	**Site**	**Mean Ct**	**SD**	**% CV**	**Mean Ct**	**SD**	**%CV**	**Mean Ct**	**SD**	**%CV**
NAP-1/B1/027	**Positive**	**1**	30.61	0.42	1.38	31.85	0.73	2.3	34.32	0.69	2.02
		2	30.58	0.51	1.65	32.16	0.8	2.5	34.43	0.71	2.05
		3	30.55	0.32	1.05	31.97	0.85	2.65	34.87	0.78	2.25
		overall	**30.58**	**0.42**	**1.37**	**32.00**	**0.80**	**2.49**	**34.53**	**0.76**	**2.19**
	Low Positive	**1**	30.63	0.4	1.3	33.38	0.71	2.14	35.58	0.55	1.55
		2	30.73	0.6	1.94	33.27	0.81	2.45	35.01	0.53	1.52
		3	30.86	0.62	2	33.07	0.84	2.53	35.45	0.69	1.96
		overall	**30.74**	**0.55**	**1.78**	**33.24**	**0.79**	**2.38**	**35.36**	**0.62**	**1.76**
	High Negative	**1**	30.71	0.35	1.15	34.21	0.54	1.58	35.88	N/A	N/A
		2	30.59	0.33	1.09	34.21	0.29	0.86	35.92	N/A	N/A
		3	30.64	0.47	1.53	34.17	0.57	1.68	N/A	N/A	N/A
		overall	**30.65**	**0.39**	**1.27**	**34.19**	**0.45**	**1.32**	**35.91**	**0.16**	**0.43**

			Internal Control			*tcdA*			*tcdB*		
Strain	**Panel Member**	**Site**	**Mean Ct**	**SD**	**% CV**	**Mean Ct**	**SD**	**%CV**	**Mean Ct**	**SD**	**%CV**
1470	**Positive**	**1**	30.67	0.49	1.58	32.22	0.86	2.67	34.74	0.61	1.76
		2	30.69	0.41	1.32	31.74	0.95	2.99	34.66	0.74	2.14
		3	30.86	0.33	1.06	31.81	0.78	2.45	34.95	0.7	2.01
		overall	**30.74**	**0.42**	**1.35**	**31.92**	**0.88**	**2.77**	**34.78**	**0.69**	**1.99**
	Low Positive	**1**	30.74	0.42	1.37	33.17	0.94	2.83	35.61	0.49	1.38
		2	30.51	0.42	1.38	33.06	0.89	2.7	35.62	0.6	1.7
		3	30.7	0.33	1.08	33.41	1.08	3.22	35.77	0.46	1.29
		overall	**30.65**	**0.4**	**1.31**	**33.2**	**0.96**	**2.9**	**35.65**	**0.53**	**1.48**
	High Negative	**1**	30.76	0.46	1.5	34.64	0.14	0.4	36.41	N/A	N/A
		2	30.55	0.45	1.46	34.15	0.28	0.83	35.82	N/A	N/A
		3	30.44	0.42	1.38	34.63	0.27	0.77	N/A	N/A	N/A
		overall	**30.58**	**0.46**	**1.49**	**34.49**	**0.31**	**0.91**	**36.12**	**0.42**	**1.16**
Negative		**1**	30.68	0.37	1.2	N/A	N/A	N/A	N/A	N/A	N/A
		2	30.66	0.47	1.55	N/A	N/A	N/A	N/A	N/A	N/A
		3	30.67	0.42	1.37	33.58	N/A	N/A	N/A	N/A	N/A
		overall	**30.67**	**0.42**	**1.36**	**33.58**	**N/A**	**N/A**	**N/A**	**N/A**	**N/A**

Target Carryover Study

Absence of carryover between samples for the entire workflow was proven by performing 5 runs with alternating high positive (formulated at a concentration which exceeded that of organisms found in 95% of specimens from diseased patients in the intended use population) and negative samples. All samples were detected correctly, generating a carryover rate of 0.0%.

Interfering Substances

A panel of 23 substances that may be present in patient specimens (Table 7) was tested to determine whether these substances interfered with the performance of the *artus* C. difficile QS-RGQ MDx Kit. Three toxigenic *C. difficile* strains: NAP-1/BI/027 strain, 1470 strain, and VPI 10463 strain, were diluted to approximately 2–3x LoD and spiked with each potentially inhibitory substance. None of the substances showed an inhibitory effect on the detection of *C. difficile* by the *artus* C. difficile QS-RGQ MDx Kit.

Table 7: Potentially Interfering Substances Tested

Type	Substance	Potential Interferent	Concentration Tested*
Anti-fungal	Miconazole nitrate cream	Miconazole nitrate	2% w/v
Cream/Suppositories	Preparation H	Hydrocortizone	2% w/v
	Zinc oxide	Zinc oxide	40% w/v
	Vaseline	Petroleum jelly	100%
Anti-hemorrhoid creams	Hemorrhoid gel	Phenylephrine hydrochloride	2% w/v
Condoms	Condoms	Nonoxynol-9	7%
Moist Towelettes	Moist Towelettes	Benzalkonium Chloride	0.12% w/v
Antacids	Gaviscon	Aluminum hydroxide, Magnesium carbonate	0.1 mg/mL
	Tums	Ca carbonate	0.5 mg/mL
	Tagamet	Cimetidine	0.5 mg/mL
	Prilosec (delayed release)	Omeprazole magnesium	0.5 mg/mL
Enemas	Mineral Oil	Mineral Oil	2% v/v
Anti-Diarrheal Medication	Imodium	Loperamide HCl	0.00667 mg/mL
	Pepto Bismol	Bismuth Subsalicylate	0.87 mg/mL
Laxative	ExLax	Sennosides	0.1 mg/mL
Antibiotics	Vancomycin HCl	Vancomycin	12.5 mg/mL
	Metronidazole	Metronidazole	14 mg/mL
Anti-inflammatory	Naproxen Sodium (Aleve)	Naproxen Sodium	14 mg/mL
Blood	Whole blood	Glucose, hormones, enzymes, iron, etc.,	5% v/v
Fecal Components	Mucus	Mucin	3 mg/mL
	Palmitic acid	Palmitic acid	2 mg/mL
	Stearic acid	Stearic acid	4 mg/mL
MRI Contrast Agents	Barium sulfate	Barium sulfate	5 mg/mL

* Represents physiologically relevant concentrations of substances

Performance Characteristics - Clinical Studies

The performance of the *artus* C. difficile QS-RGQ MDx Kit was evaluated at 3 external testing sites using *C. difficile* patient samples from 5 geographically diverse locations within the United States in 2013. The *artus* C. difficile QS-RGQ MDx Kit was compared to direct and/or enriched culture. The tables below present the data from these studies.

Assay vs. Direct and Enriched Culture Comparison

A total of 759 liquid or soft stool specimens were collected from patients suspected of having *Clostridium difficile*-associated disease. Ten (10) specimens were missing *artus* and culture results and were withdrawn from the study. Of the 749 specimens with *artus* results reported, sixteen (16) specimens reported an invalid result (2.14%) with the *artus* C. difficile QS-RGQ MDx Kit. Of these samples, 8 returned valid results upon retesting (all negative) and 8 reported a final invalid result for the *artus* C. difficile QS-RGQ MDx Kit (1.07%). The remaining 741 specimens with valid *artus* results were included in the final data set and analyzed for product performance.

Assay vs. Enriched Culture Comparison

A total of 741 specimens were tested by both the *artus* C. difficile QS-RGQ MDx Kit and enriched toxigenic culture. The overall assessment of sensitivity and specificity versus enriched toxigenic culture is shown in Table 8.

Table 8: Clinical Performance of *artus* C. difficile QS-RGQ MDx Kit vs. Enriched Toxigenic Culture

Combined Sites – Combined Ages				
		Enriched Toxigenic Culture		
		Positive	Negative	Total
artus C. difficile QS-RGQ MDx Kit	Positive	114	17*	131
	Negative	13**	597	610
	Total	127	614	741

		95% CI
Sensitivity	90%	83% – 94%
Specificity	97%	96% – 98%
Positive Predictive Value	87%	80% – 92%
Negative Predictive Value	98%	96% – 99%
Prevalence	17%	15% – 20%

*17 discordant specimens (*artus* C. difficile QS-RGQ MDx Positive, Enriched Toxigenic Culture Negative) reported were analyzed by alternative PCR followed by bi-directional sequencing and the result was that 12 out of 17 were positive for toxigenic *C. difficile*, agreeing with the artus C. difficile QS-RGQ MDx result.

** 12 discordant specimens (*artus* C. difficile QS-RGQ MDx Negative, Enriched Toxigenic Culture Positive) reported were analyzed by alternative PCR followed by bi-directional sequencing and the result was that 10 out of 12 were negative for toxigenic *C. difficile*, agreeing with the *artus* C. difficile QS-RGQ MDx result. The remaining 1 discordant specimen was unavailable for testing.

Assay vs. Direct Toxigenic Culture Comparison

There were a total of 699 specimens for which a direct toxigenic culture result was available. The overall assessment of sensitivity and specificity versus direct toxigenic culture is shown in Table 9.

Table 9: Clinical Performance of *artus* C. difficile QS-RGQ MDx Kit vs. Direct Toxigenic Culture

Combined Sites – Combined Ages				
		Direct Toxigenic Culture		
		Positive	Negative	Total
***artus* C. difficile QS-RGQ MDx Kit**	Positive	84	21*	105
	Negative	1**	593	594
	Total	85	614	699

		95% CI
Sensitivity	99%	94% – 100%
Specificity	97%	95% – 98%
Positive Predictive Value	80%	71% – 87%
Negative Predictive Value	100%	99% – 100%
Prevalence	12%	10% – 15%

*19 discordant specimens (*artus* C. difficile QS-RGQ MDx Positive, Direct Toxigenic Culture Negative) reported were analyzed by alternative PCR followed by bi-directional sequencing and the result was that 14 out of 19 were positive for toxigenic *C. difficile*, agreeing with the *artus* C. difficile QS-RGQ MDx result. The remaining 2 specimens were unavailable for testing.

**The 1 discordant specimen (*artus* C. difficile QS-RGQ MDx Negative, Direct Toxigenic Culture Positive) was unavailable for testing.

Conclusions

The *artus*® C. difficile QS-RGQ MDx Kit is substantially equivalent to the legally marketed Quidel Molecular Direct C. difficile Assay.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

QIAGEN GMBH
KIMBERLY MAPP, Ph.D
MANAGER, REGULATORY AFFAIRS
1201 CLOPPER ROAD
GAITHERSBURG MD 20878

April 4, 2014

Re: K133936
Trade/Device Name: artus C. difficile QS-RGQ MDx Kit
Regulation Number: 21 CFR 866.3130
Regulation Name: Clostridium difficile toxin gene amplification assay
Regulatory Class: II
Product Code: OZN, OOI
Dated: January 6, 2014
Received: January 6, 2014

Dear Dr. Mapp:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Uwe Scherf -S for

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K133936

Device Name
artus® C. difficile QS-RGQ MDx Kit

Indications for Use *(Describe)*
The artus C. difficile QS-RGQ MDx Kit is an in vitro polymerase chain reaction (PCR) assay for use on the QIAsymphony RGQ MDx system for the qualitative detection of toxigenic Clostridium difficile toxin A and toxin B genes in human liquid or soft stool specimens from patients suspected of having Clostridium difficile associated disease. The test is intended to be used directly on patient samples.

The artus C. difficile QS-RGQ MDx Kit is intended to be used to aid in diagnosis of Clostridium difficile infection.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Ribhi Shawar -S
2014.04.01 07:31:29 -04'00'

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

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Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."